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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,023	12/11/2003	Anne Vanet	1421-03	2355
35811 7590 02/19/2008 IP GROUP OF DLA PIPER US LLP ONE LIBERTY PLACE 1650 MARKET ST, SUITE 4900 PHILADELPHIA, PA 19103				
EXAMINER				
SKOWRONEK, KARL HEINZ R				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/734,023

Applicant(s)

VAN ET AL.

Examiner

KARLHEINZ R. SKOWRONEK

Art Unit

1631

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 11-19, 21-27, 30 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 20, 28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/06)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

Claim Status

Claims 1-31 are pending.

Claims 11-19, 21-27, and 30-31 stand withdrawn as being directed to a non-elected invention.

Claims 1-10, 20, 28, and 29 are being examined.

Non-compliant amendment

It is noted that the amendment file 30 November 2007 is non-compliant with respect to 37 CFR 1.121(c). Claims 11-19, 21-27, and 30-31 stand withdrawn, however the claims filed 30 November 2007 fail to indicate the proper status of the claims, i.e. withdrawn. Applicant is requested to verify that future amendments to the claims indicate the correct status of the claims and that any amendments made conform to 37 CFR 1.121.

Specification

Response to Arguments

Applicant's arguments, see remarks p. 17, filed 30 November 2007, with respect to the objections to the specification for having embedded hyper links have been fully considered and are persuasive. The objection to the specification has been withdrawn.

Claim Objections

Response to Arguments

Applicant's arguments, see remarks p. 17, filed 30 November 2007, with respect to the objections of claim 6 have been fully considered and are persuasive. The objection to claim 6 has been withdrawn.

Claim Rejections - 35 USC § 112, Second Paragraph

Response to Arguments

Applicant's arguments, see remarks p. 17, filed 30 November 2007, with respect to the rejection of claim 6 under 35 USC 112, second paragraph have been fully considered and are persuasive. The rejection of claim 6 has been withdrawn.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NEW MATTER

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Claim 6 recites "positions i, j, or k". The definition of j as a position is new matter. The variable, j, has been defined as a sequence at [0043] in the specification as originally filed. By redefining it as a position in line 2 of claim 6, applicant has introduced new matter. The examiner suggests an amendment to claim 6 lines 2-5 as follows as potential language to overcome this rejection, "...numerical matrix A of dimensions NxM in which j designates a sequence of N number of sequences and i or k designates a motif of M number of motifs of a sequence of said alignment and i or k and j are paired, corresponding to a column number and line number in the first numerical matrix...".

Enablement

Claims 1-10, 20, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Although claims 11-19 have not been examined, it is noted that withdrawn claims 11-19 are similarly not enabled.

In the decision of *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the

nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must be able to identify either nucleotide or amino acid residues within a set of sequences that have or have not mutated simultaneously. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The description describes comparison of sets of sequences using algorithms known in the sequence comparison art. The description does not provide detailed guidance to identify residues between sequences of set that have or not mutated simultaneously. The description does not describe methodology for determining from an alignment whether a subset of sequences the set mutated simultaneously. The disclosure does not provide guidance for identifying mutated and non-mutated couples.

c) The description provides working examples of sequence comparison analysis to identify residues that differ between a query sequence and a reference sequence using an identity matrix. The description does not provide working examples of determining from an alignment, residues of a subset of sequences that mutated simultaneously. The description does not provide an example of how to mutated couples are identified

d) The nature of the invention, phylogenetic sequence comparison, is complex.

e) The prior art does not show methodology or algorithms for the determination of simultaneous mutation between sequences using sequence comparison methods. The

art, at the time the invention was made, is silent regarding the timing at which mutations occur in sequences based on sequence alignment data. Rose et al. (Bioinformatics, Vol.16, No. 4, p. 400-401, 2000) discusses the identification of hypermutations, an extreme form of mutation, in sequences. Rose et al. are silent with respect to mutations among sequences occurring simultaneously. Strimmer et al. (PNAS Vol. 94, p. 6815-6819, June 1997) discuss a method for studying the phylogenetic content of sequence alignments. While Strimmer et al. show that biological sequence data can be analyzed for phylogenetic data; they are silent on the timing of mutations, specifically if mutations occurred simultaneously. Strimmer et al. also teach that it may not always be possible to resolve the phylogenetic relationships between sequences (p. 6815, col. 2). Caride et al. (Journal of Clinical Virology, vol. 23, p. 179-189, 2002) demonstrate the method Rose et al. as applied to HIV-1 isolates and sequences of the HIV protease. Caride et al. demonstrate the hypermutability of the protease gene. Caride used phylogenetic inference to analyze sequences (figure 4). However, Caride et al. are silent with respect to mutations occurring simultaneously.

f) The skill of those in the art of phylogenetic sequence comparison is high.

g) The predictability of determining if mutations found in at least 2 sequences occurred simultaneously or not is unknown in the prior art.

h) The claims are broad in that the claims are drawn to a method of identifying residues in any sequence within a set of sequences that have mutated simultaneously with respect to at least one other sequence.

The skilled practitioner would first turn to the instant description for guidance in

using the claimed invention. However, the description lacks clear evidence of methodology for identifying at least 2 sequences in which a mutation has occurred simultaneously. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss methods or algorithms for identifying if residues within sequences mutated simultaneously. Finally, said practitioner would turn to trial and error experimentation to determine a relationship that can be employed to elucidate markers or identifiers that indicate a mutation had occurred simultaneously in two different sequences. Such amounts to undue experimentation.

Response to Arguments

Applicant's arguments filed 30 November 2007 have been fully considered but they are not persuasive.

Applicant argues that the determination of mutations that have mutated simultaneously would not require undue experimentation and that one of skill in the art is enabled to identify mutations that mutated simultaneously. This is not persuasive. Applicant has not provided evidence to refute the finding in the art that it is not always possible to resolve the phylogenetic relationships between sequences and that the art is silent with respect to the timing of mutations as occurring simultaneous. It is undue experimentation for one skilled in the art to develop a method of determining the timing of mutations to identify mutations that occurred simultaneously where the art identifies difficulties in determining the timing of mutation or resolve the phylogenetic relationships between sequences. Applicant incorrectly refers to Korber et al as being cited in the previous office action however no reference entitled Korber et al was actually cited in

the previous office action. Applicant cites Korber et al. to show an example of classical sequence comparison in the remarks filed 30 November 2007. Korber et al. shows functional studies of the V3 loop depend on making simultaneous mutation via site directed mutagenesis (p. 7179, col. 2). Making simultaneous mutation via site directed mutagenesis is distinct from determining through sequence comparison, i.e. phylogenetics, that two mutations occurred simultaneously. Thus, Korber et al. is silent on the identification and determination of mutations that occurred simultaneously.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone

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number is (571)272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

19 February 2008

/K. R. S./

Examiner, Art Unit 1631